REMARKS/ARGUMENTS

This amendment is filed in response to the Office Action mailed October 16, 2008 for the above captioned application. Reconsideration of the application as amended in view of the remarks herein and the declaration under Rule 132 filed herewith is respectfully requested.

Applicants request an extension of time sufficient to make this paper timely and enclose the fee.

Applicants note the examiner's extensive comments on how to make a drawing correction. It is understood, however, that the desired result of removing drawing sheet 11 from the application has been accomplished and that no further amendments to the drawings are necessary. Should this understanding be in error, clarification is requested.

The Examiner objected to the specification, stating that the Brief Description of the Drawings still referred to Figs 12A and 12B and that an amendment was necessary. Applicants point out that the entire section was amended in the preliminary amendment filed with the application on 5/27/2005 and this change was made therein. This shows as amendments to the specification in the PAIR Image File Wrapper. No additional amendment is believed to be required.

Some withdrawn claims have been canceled without prejudice to Applicants' right to pursue these claims in a timely filed divisional application.

New independent claims 200 and 202 have been added reciting binding partners comprising the specific VH sequence options set forth in claims 134 separately. Claims 201 and 203 list the VL options as found in claim 135.

Applicants thank the Examiner for the helpful comments and suggestions relating to this application. Applicants have heeded these comments in focusing the claims on specifically identified characteristics of the antibodies.

Claim 121 has been amended to specifically recite two characteristics of patient serum TSH receptor autoantibodies that are present in the claimed antibodies, namely inhibition of TSH binding to the TSH receptor and stimulation of cAMP production by cells expressing the TSH receptor. These limitations were previously found individually in claims 125 and 128 and in combination in claim 131. Redundant claims have been canceled and dependency has been corrected.

Claims 121, 122, 125, 128 and 131 were rejected as anticipated by WO 91/09137. WO 91/09137 discloses a sequence for a recombinant TSH receptor and states on Page 39 that one could make monoclonal antibodies using this recombinant receptor as an antigen. There is no teaching of any specific monoclonal antibody, nor may it be inferred that a monoclonal antibody would necessarily have the properties now recited in the claims. Accordingly, this general statement is not sufficient for an anticipation rejection. As the Examiner has noted, Example VIII shows autoantibodies that include the properties recited in amended claim 121. These autoantibodies are neither monoclonal nor recombinant, and the characteristics could easily arise from separate components in a polyclonal mixture. Lines 7 to 32 on page 101 refer to two different types of TSH autoantibodies – those that stimulate cAMP production, and, separately, those that inhibit TSH binding to the TSH receptor. It is noted that both types of autoantibodies may be present in the same patient. However, there is no indication whatsoever that both activities may be present in a single autoantibody – there is no teaching or suggestion of patient autoantibodies possessing both the characteristics required by claim 121. On this basis, therefore, the skilled person would understand that the results presented in this Example, in terms of stimulation of cAMP production and inhibition of TSH binding, arise from separate antibodies. Therefore the results presented are insufficient to establish a teaching of an anticipatory antibody within the scope of the present claims. Accordingly, withdrawal of this rejection is respectfully urged.

Claims 121, 122, 128 and 199 also stand rejected as anticipated Akamizu et al. It is noted that this rejection was not applied to claim 131. Accordingly, since the limitations of claim 131 have now been incorporated into claim 121, this rejection is believed to be overcome. Nevertheless, Applicants address the evidence that the antibodies of Akamizu do not have both properties in the enclosed Declaration Under Rule 132, ¶ 7).

Claims 121, 122, 125-133 and 199 stand rejected as anticipated by Kohn et al. ¶¶ 8-10 of the enclosed Declaration relate to the Kohn reference and explain why this reference does not meet the limitations of the claim as now presented, or of claim 131 as previously presented. In this regard, Applicants further note that while the present claims (and previous claim 131) require inhibition of TSH binding and stimulation of cAMP production. Table 4, to which the Examiner refers, does not appear to show this. In fact, this Table relates to the ability of a TBII (a binding inhibitor) to inhibit stimulation of cAMP production caused by TSH or Graves IgG.

Claims 136 and 137 were rejected as obvious over the combination of van der Heijden, Kohn along with additional evidence. van der Heijden recites antibody fragments which the Examiner acknowledges lack inhibitory activity with respect to TSH binding or stimulatory activity with respect to cAMP production. Thus, these antibodies do not fall within the limitations of the present claims. The Examiner then cites Kohn and recites characteristics of the antibodies. As noted above, these antibodies also do not meet the limitations of the claims

because they do not have both of the required characteristics. Thus, the combination of the cited references fail to provide suggestion of the claimed invention as set forth in claims 136 and 137, because at best they would provide alternative methods to make antibodies or fragments lacking in the recited characteristics of Graves' disease autoantibodies.

Claim 125 was rejected under 35 USC § 112, second paragraph. This claim has been canceled, rendering the rejection moot.

Claims 121, 122, 125-137, 198 and 199 were rejected as indefinite because of the alternative statement "derived from." This has been deleted from claim 121, and this is believed to overcome this rejection.

Finally, with respect to the non-elected claims remaining in the application, Applicants submit that there is unity of invention between these claims and elected claims including claim 121. Therefore recombination of these claims in this application is requested. Specifically,

(1) withdrawn method claim 162, as amended, is a method for making human monoclonal antibodies with the same characteristics as the antibodies of claim 121.

(2) claims 168, 173, 174, and 193-195 have been amended to refer only to claim 121 and provide methods of using the binding partners of that claim, and include related claim steps.

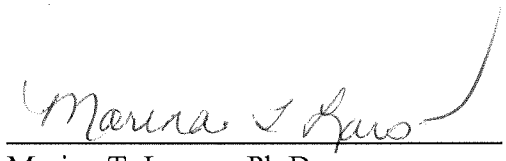
(3) claims 175 and 176 has been been amended to refer only to claim 121 and provides a further method of using the binding partners of that claim to identify epitopes or binding sites of the TSH receptor.

(4) Claims 177 - 179 and 182-188 relate to anti-idiotypes of the binding partners of claim 121. Since the binding partner is necessary to making the anti-idiotype, there should be unity of invention.

(5) Claims 189 and 192 and the claims dependent thereon relate to combinations of the binding partner of claim 121, and another material. Since a composition comprising a material that is novel and unobvious should itself be novel and unobvious, it follows that these claims should be included in this application.

For the foregoing reasons, Applicants submit that this application is now in form for allowance. Should there be minor matters which might be resolved by telephone to achieve allowance, the Examiner is encouraged to call the undersigned.

Respectfully submitted,



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